Complete Summary

GUIDELINE TITLE

Evaluation of asymptomatic microscopic hematuria in adults: the American Urological Association best practice policy. Parts I and II.

BIBLIOGRAPHIC SOURCE(S)

Grossfeld GD, Litwin MS, Wolf JS Jr, Hricak H, Shuler CL, Agerter DC, Carroll PR. Evaluation of asymptomatic microscopic hematuria in adults: the American Urological Association best practice policy--part II: patient evaluation, cytology, voided markers, imaging, cystoscopy, nephrology evaluation, and follow-up. Urology 2001 Apr;57(4):604-10. [32 references]

Grossfeld GD, Litwin MS, Wolf JS, Hricak H, Shuler CL, Agerter DC, Carroll PR. Evaluation of asymptomatic microscopic hematuria in adults: the American Urological Association best practice policy--part I: definition, detection, prevalence, and etiology. Urology 2001 Apr;57(4):599-603. [29 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Asymptomatic microscopic hematuria

GUIDELINE CATEGORY

Diagnosis
Evaluation

CLINICAL SPECIALTY

Family Practice
Internal Medicine

Nephrology
Obstetrics and Gynecology
Urology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To formulate best practice recommendations for the detection and evaluation of asymptomatic microscopic hematuria
- To serve as guidance to urologists and primary care physicians with respect to the evaluation of adult patients who may have asymptomatic microscopic hematuria

TARGET POPULATION

Adults with asymptomatic microscopic hematuria

INTERVENTIONS AND PRACTICES CONSIDERED

1. Patient history
2. Physical examination, including urethral and vaginal examination for women and retraction of foreskin to expose glans penis in uncircumcised men
3. Collection of urine specimen (freshly voided, clean-catch, midstream)
4. Quantitative measurement of hematuria, such as chamber count (number of red blood cells per milliliter of urine excreted); sediment count (direct examination of centrifuged urinary sediment); or dipstick examination
5. Laboratory analysis, including comprehensive examination of urine and urinary sediment, number of red blood cells per high-powered field, presence of dysmorphic red blood cells or red blood cell casts, presence and degree of proteinuria, evidence or urinary tract infection, and level of serum creatinine
6. Radiologic imaging of upper urinary tracts
7. Cystoscopic evaluation of the urinary bladder
8. Voided urinary cytology
9. Evaluation of voided urinary markers
10. Intravenous urography
11. Ultrasonography
12. Computed tomography, with or without contrast enhancement
13. Magnetic resonance imaging, with or without contrast enhancement
14. Referral to nephrologist
15. Follow-up

MAJOR OUTCOMES CONSIDERED

- Level of microscopic hematuria (number of red blood cells per high-power microscopic field)
- Sensitivity, specificity, and positive/negative predictive value of various voided urine tests for detection of bladder cancer

- Sensitivity of imaging tests, such as intravenous urography, ultrasound, computed tomography, and magnetic resonance imaging
- Diagnostic accuracy of rigid and flexible cystoscopy

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The panel formulated its policy statements and recommendations by consensus, on the basis of a review of published reports and panel members´ own expert opinions.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

After the Best Practice Policy Panel on Asymptomatic Microscopic Hematuria reached an initial consensus, the manuscript was circulated to 85 peer reviewers representing the following medical specialties: family practice, internal medicine, radiology, nephrology, and urology. Comments were received from 55 peer reviewers, and the panel made numerous changes to the document to incorporate the suggested concepts the panel considered to be warranted.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Excerpted by the National Guideline Clearinghouse (NGC)

Detection and Definition of Microscopic Hematuria

The initial determination of microscopic hematuria should be based on microscopic examination of the urinary sediment from a freshly voided, clean-catch, midstream urine specimen.

Hematuria can be measured quantitatively by: (1) determining the number of red blood cells (RBCs) per mL of urine excreted (chamber count), (2) direct examination of the centrifuged urinary sediment (sediment count), or (3) indirect examination of the urine by dipstick - the simplest way to detect microscopic hematuria. Given the limited specificity of the dipstick method (65 to 99 percent for 2 to 5 red blood cells per high-power microscopic field), however, the initial finding of microscopic hematuria should be confirmed by microscopic evaluation of urinary sediment.

The recommended definition of microscopic hematuria is $\geq$3 red blood cells/high-power field on microscopic evaluation of the urinary sediment from two of three properly collected urinalysis specimens. Before deciding to defer an evaluation in patients with 1 or 2 red blood cells/high-power field, risk factors for significant disease should be taken into consideration. High-risk patients should be considered for a full urologic evaluation after one properly performed urinalysis documenting the presence of at least 3 red blood cells/high-power field. Risk factors for significant disease in patients with microscopic hematuria include the following:

- Smoking history
- Occupational exposure to chemicals or dyes (benzenes or aromatic amines)
- History of gross hematuria
- Age older than 40 years
- History of urologic disorder or disease
- History of urinary tract infection
- Analgesic abuse
- History of pelvic irradiation

Prevalence of Asymptomatic Hematuria

The prevalence of asymptomatic microscopic hematuria varies from 0.19 percent to as high as 21 percent.

Differences in the age and sex of populations screened, amount of follow-up, and number of screening studies per patient account for this range.

Patient Evaluation

Patients with asymptomatic microscopic hematuria who are at risk for urologic disease or primary renal disease should undergo an appropriate evaluation. In patients at low risk for disease, some components of the evaluation may be deferred (see Figure 1 in the original guideline document [Part II] and Figures 1 and 2 in the American Academy of Family Physician´s summary of the original guideline document [Grossfeld GD, Wolf JS Jr, Litwin MS, Hricak H, Shuler CL, Agerter DC, Carroll PR. Asymptomatic microscopic hematuria in adults: summary of the AUA best practice policy recommendations. Am Fam Physician 2001 Mar 15;63(6):1145-54]).

Asymptomatic microscopic hematuria has many causes ranging from minor, incidental findings that do not require treatment to highly significant lesions that are immediately life-threatening. Therefore, hematuria has been classified into four categories: life-threatening, highly significant requiring treatment, highly significant requiring observation, and insignificant (see Table 1 titled "Reported Causes of Asymptomatic Microscopic Hematuria" in the original guideline document [Part 1] for a complete listing.)

Indications for Nephrology Evaluation

The presence of significant proteinuria, red cell casts or renal insufficiency and/or a predominance of dysmorphic red cells in the urine should prompt an evaluation for renal parenchymal disease or referral to a nephrologist.

Significant proteinuria is defined as a total protein excretion of greater than 1,000 mg per 24 hours (1g per day), or greater than 500 mg per 24 hours (0.5 g per day) if protein excretion is persistent or increasing, or if there are other factors suggest the presence of renal parenchymal disease. In the absence of massive bleeding, a total protein excretion in excess of 1,000 mg per 24 hours would be unlikely and should prompt a more extensive evaluation or nephrology referral.

Red cell casts are virtually pathognomonic for glomerular bleeding. Unfortunately, they are a relatively insensitive marker. It is, therefore, useful to examine the character of the red cells. Dysmorphic urinary red blood cells show variation in size and shape and usually have an irregular or distorted outline. Such red blood cells are generally glomerular in origin. In contrast, normal doughnut-shaped red blood cells are generally due to lower urinary tract bleeding. Accurate determination of red blood cell morphology may require inverted phase contrast microscopy.

The percentage of dysmorphic red blood cells required to classify the hematuria as glomerular in origin has not been adequately defined. Glomerular bleeding is associated with more than 80 percent dysmorphic red cells, and lower urinary tract bleeding with more than 80 percent normal red blood cells. Percentages falling between these ranges are indeterminate and could represent bleeding from either source.

The initial evaluation of the urinary sediment generally identifies those patients with parenchymal renal disease. Glomerular disease is most likely in this setting and may be associated with a variety of systemic diseases including lupus, vasculitis, malignancy, and infections such as hepatitis and endocarditis. Glomerular diseases localized to the kidney include membranoproliferative glomerulonephritis, immunoglobulin A (IgA) nephropathy, and crescentic glomerulonephritis. In addition, interstitial renal disease, such as drug-induced interstitial disease and analgesic nephropathy, may be associated with hematuria. If systemic causes are not identified, renal biopsy is usually recommended.

Patients with microscopic hematuria, a negative initial urologic evaluation, and no evidence of glomerular bleeding are considered to have isolated hematuria. Although many such patients may have structural glomerular abnormalities, they appear to have low risk of progressive renal disease. Thus, the role of renal biopsy in this setting has not been defined. Nevertheless, because data on follow-up is limited, these patients should be followed for the development of hypertension, renal insufficiency, or proteinuria.

Urologic Evaluation

In patients without risk factors for primary renal disease, a complete urologic evaluation should be performed.

Complete urologic evaluation of microscopic hematuria includes a history and physical examination, laboratory analysis, and radiologic imaging of the upper urinary tract followed by cystoscopic examination of the urinary bladder. In some cases, cytologic evaluation of exfoliated cells in the voided urine specimen may also be performed. If a careful history suggests a potential "benign" cause for microscopic hematuria, the patient should undergo repeat urinalysis 48 hours after cessation of this activity. No additional evaluation is warranted if the hematuria has resolved. Patients with persistent hematuria require evaluation.

In women, physical examination should include a urethral and vaginal examination to exclude any local causes of microscopic hematuria. A catheterized urinary specimen is indicated if a clean catch specimen cannot be reliably obtained (i.e., vaginal contamination, obese patients). In uncircumcised men, the foreskin

should be retracted to expose the glans penis, if possible. If a phimosis is present, a catheterized urinary specimen may be required.

The laboratory analysis begins with comprehensive examination of the urine and urinary sediment. The number of red blood cells per high-powered field should be determined. In addition, the presence of dysmorphic red blood cells or red cell casts should be noted. The urine should also be tested for the presence and degree of proteinuria and any evidence of urinary tract infection. Patients with urinary tract infection should be treated appropriately, and the urinalysis should be repeated 6 weeks after treatment. If the hematuria resolves after treatment, no additional evaluation is necessary. Serum creatinine should be measured. The remaining laboratory investigation should be guided by any specific findings on history, physical examination, and urinalysis.

Voided Urinary Cytology and Urinary Markers

Urothelial cancers, the target of a cytologic examination, are the most commonly detected malignancies in patients with microscopic hematuria.

Voided urinary cytology is recommended for all patients with risk factors for transitional cell carcinoma. This test can be a useful adjunct to cystoscopic evaluation of the bladder, especially in the determination of carcinoma-in-situ. For asymptomatic microscopic hematuria patients without risk factors for transitional cell carcinoma, urinary cytology or cystoscopy may be used. If cytology is chosen and malignant or atypical/suspicious cells are identified, cystoscopy is required since the presence of hematuria is a significant risk factor for malignancy in such patients.

Several recently identified voided urinary markers have been examined for the early detection of bladder cancer. At this time, there are insufficient data available to recommend their routine use in the evaluation of patients with microscopic hematuria. Further studies are warranted to determine their role in the diagnostic evaluation of such patients.

Imaging Studies

Intravenous urography (IVU), ultrasonography, and computed tomography (CT) are used to evaluate the urinary tract in patients with microscopic hematuria. Because of lack of impact data, evidence-based imaging guidelines cannot be formulated.

Intravenous urography currently remains the initial evaluation of choice for upper tract imaging in patients with microhematuria because (1) the technology is standardized, (2) previous series examining patients with microhematuria have been based on this modality, (3) there is a low rate of missed diagnoses when intravenous urography is followed by appropriate studies, and (4) intravenous urography is less expensive than computed tomography in most centers. However, the advantage of computed tomography over intravenous urography is that computed tomography has the highest efficacy for the range of possible underlying pathologies, and it shortens the duration of a diagnostic work-up.

If computed tomography is chosen as the initial upper tract study, the imaging protocol should be adapted to the diagnostic goals such as exclusion of urolithiasis and renal neoplasm. Computed tomography urography spiral (helical) is preferred if the technology is available. Neither oral nor rectal contrast media is required. The computed tomography protocol should start with a noncontrast scan. If this scan demonstrates urolithiasis in a patient who is at low-risk for underlying malignancy, then no further scanning is needed. In all other patients, including those in whom a urinary calculus is not detected, intravenous contrast should be injected. Computed tomography scout (topogram) or plain abdominal radiography (depending on the equipment available) can be taken at the end of the computed tomography examination to assess the ureters and bladder in an intravenous urography-like fashion.

Cystoscopy

Cystoscopic evaluation of the bladder - complete visualization of the bladder mucosa, urethra and ureteral orifices - is necessary to exclude the presence of bladder cancer.

Cystoscopy as a component of the initial office evaluation of microscopic hematuria is recommended for all adults over age 40 and those under age 40 with bladder cancer risk factors. This includes patients in whom upper tract imaging reveals a potential benign source for bleeding. Cystoscopy appears to have a low yield in select patients at low risk for bladder cancer including men and women under 40 with no bladder cancer risk factors. In these patients, initial cystoscopy may be deferred, but urinary cytology should be obtained.

Initial diagnostic cystoscopy can be performed under local anesthesia using either a rigid or flexible cystoscope. Compared with rigid cystoscopy, flexible cystoscopy causes less pain and is associated with fewer post-procedure symptoms. In addition, positioning and patient preparation are simplified, and procedure time is reduced. Flexible cystoscopy appears to be at least equivalent in diagnostic accuracy to rigid cystoscopy; and for some lesions (i.e., those at the anterior bladder neck), it may be superior. Flexible cystoscopy has been widespread in the United States since the early 1990s. Therefore, some urologists may not have adequate experience with the technique.

Follow-up

Because some patients with a negative initial evaluation for asymptomatic microhematuria eventually develop significant urologic disease, some form of follow-up is indicated.

Although most patients with a negative initial evaluation for asymptomatic microhematuria do not develop significant urologic disease, some patients do. Consequently, some form of follow-up is indicated. Because the appearance of hematuria can precede the diagnosis of bladder cancer by many years, such follow-up seems especially important for high-risk groups, including patients over 40 and those who use tobacco or whose occupational exposures put them at risk. Because the risk of life-threatening lesions in patients with a negative initial evaluation is low and the data regarding follow-up in such patients is sparse,

recommendations regarding appropriate follow-up must be based on consensus opinion, in addition to review of the available literature-based evidence.

For patients with a negative initial evaluation of asymptomatic microscopic hematuria, consideration should be given to repeating a urinalysis, voided urine cytology and blood pressure determination at 6, 12, 24 and 36 months. Although cytology may not be a sensitive marker for detecting low-grade transitional cell carcinoma, it will detect most high-grade tumors and carcinoma-in-situ, particularly if the test is repeated. Such high-grade lesions are the most likely to benefit from early detection.

Additional evaluation, including repeat imaging and cystoscopy may be warranted in patients with persistent hematuria in whom there is a high index of suspicion for significant underlying disease. In this setting, the clinical judgment of the treating physician should guide any further evaluation. Immediate urologic re-evaluation, with consideration of cystoscopy, cytology and/or repeat imaging, should be obtained if any of the following occur: (1) gross hematuria, (2) abnormal urinary cytology, or (3) irritative voiding symptoms in the absence of infection. If none of these occur within 3 years, the patient does not require further urologic monitoring. Further evaluation for renal parenchymal disease or referral to a nephrologist should be considered if hematuria persists and either hypertension, proteinuria, or evidence of glomerular bleeding (red cell casts, dysmorphic red blood cells) develops.

CLINICAL ALGORITHM(S)

The original guideline contains clinical algorithms for suggested follow-up regimens for low-risk and high-risk patients with asymptomatic microscopic hematuria and an initial negative urologic evaluation. The companion document contains clinical algorithms for initial evaluation of asymptomatic microscopic hematuria and urologic evaluation of asymptomatic microscopic hematuria.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate detection and evaluation of asymptomatic microscopic hematuria in adults
- Identification of significant or life-threatening urologic diseases, including malignancies, allowing for appropriate treatment or follow-up

Subgroups Most Likely to Benefit:

Patients with underlying life-threatening diseases (e.g., bladder or renal cell cancers or other malignancies) or significant diseases requiring treatment.

POTENTIAL HARMS

Diagnostic cystoscopy using rigid or flexible cystoscopes can cause pain and may be associated with post-procedure symptoms.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Grossfeld GD, Litwin MS, Wolf JS Jr, Hricak H, Shuler CL, Agerter DC, Carroll PR. Evaluation of asymptomatic microscopic hematuria in adults: the American Urological Association best practice policy--part II: patient evaluation, cytology, voided markers, imaging, cystoscopy, nephrology evaluation, and follow-up. Urology 2001 Apr;57(4):604-10. [32 references]

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Apr

GUIDELINE DEVELOPER(S)

American Urological Association, Inc. - Medical Specialty Society

SOURCE(S) OF FUNDING

American Urological Association, Inc. (AUA)

GUIDELINE COMMITTEE

Best Practice Policy Panel on Asymptomatic Microscopic Hematuria

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Authors: Gary D. Grossfield; Mark S. Litwin; Stuart Wolf, Jr.; Hedvig Hricak; Cathryn L Shuler; David C. Agerter; Peter R. Carroll

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

An update is not in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Not available at this time.

Print copies: Available from the American Urological Association, Inc., 1000 Corporate Boulevard, Linthicum, MD 21090.

AVAILABILITY OF COMPANION DOCUMENTS

The following summary is available at the American Academy of Family Physicians Web site in HTML Format and in Portable Document Format (PDF).

- Grossfeld GD, Wolf JS Jr, Litwin MS, Hricak H, Shuler CL, Agerter DC, Carroll PR. Asymptomatic microscopic hematuria in adults: summary of the AUA best practice policy recommendations. Am Fam Physician 2001 Mar 15;63(6):1145-54.

Print copies: Available from the American Academy of Family Physicians, Inc., 11400 Tomahawk Creek Parkway, Leadwood, KS 66211-2672

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on November 7, 2001. The information was verified by the guideline developer as of December 24, 2001.

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